UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,472	12/14/2001	Christopher Kern	02481.1767	1068

22852 7590 10/14/2005

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,472	KERN ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 26-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8 and 26-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on December 19, 2002 is acknowledged. The requirement was made FINAL in the Office Action dated March 26, 2003.

Applicant's Response Dated August 8, 2005

2. In the Response filed August 8, 2005, claims 31-37 were added. Claims 1, 3-8, and 26-37 are pending. An action on the merits of claims 1, 3-8, and 26-37 is contained herein below.

3. The rejection of claims 1, 4 and 6-8 under 35 U.S.C. 102(b) as being anticipated by Yeda Research and Development WO 92/19249 (Yeda) is maintained for the reasons of record as set forth in the Office Action dated March 31, 2005.

4. The rejection of claims 3, 5, and 26-30 under 35 U.S.C. 103(a) as being unpatentable over Yeda Research and Development WO 92/19249 (Yeda) and Claiborne et al. US 6,291,457 (Claiborne) in combination is maintained for the reasons of record as set forth in the Office Action dated March 31, 2005.

Rejections of Record Set Forth in the Office Action Dated March 31, 2005

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 4 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yeda Research and Development WO 92/19249 (Yeda).

Applicant's arguments filed August 8, 2005 have been fully considered but they are not persuasive. Applicant has maintained the argument that Yeda does not disclose the treatment of any of the conditions recited in the rejected claims.

The examiner respectfully disagrees with applicant's assertion. Yeda discloses the administration of low molecular weight heparin (LMWH) compositions for the prevention and/or treatment of pathological process involving the induction of TNF-α secretion, including rheumatoid arthritis (page 7, lines 9-30; page 8, lines 1-18; page 11, lines 27-34). LMWH disclosed by Yeda includes enoxapirin in doses of 20 mg / 0.2 ml and 40 mg / 0.4 ml of water. The compositions are administered in any manner as dictated by the particular application at hand including, but not limited to, enteral administration (including oral) or parenteral administration (including topical or inhalation with the aid of aerosols). In preferred embodiments, the compositions are administered subcutaneously or intravenously.

In construing process claims and references, it is the identity of manipulative operations which leads to finding of anticipation. In the instant case, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. Rheumatoid arthritis is a disorder involving a disturbance of bone metabolism, and one of ordinary skill in the art at the time of the invention would have been aware of such.

7. Claims 3, 5 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeda Research and Development WO 92/19249 (Yeda) and Claiborne et al. US 6,291,457 (Claiborne) in combination.

Applicant's arguments filed August 8, 2005 have been fully considered but they are not persuasive. Applicant argues that there is no motivation to combine the cited references or reasonable expectation of success. Applicant further suggests that the only disorder recited in applicant's claims that is included in the Claiborne is myalgia. Applicant further contends that Claiborne, by implication, conveys that the various forms of arthritis are not mediated by TNF.

The examiner disagrees with applicant's characterization of the prior art. Applicant's attention is directed to column 1, lines 40-52, of Claiborne wherein Claiborne explicitly teaches, "Excessive or unregulated tumor necrosis factor (TNF) production or activity has been implicated in mediating or exacerbating rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, and other arthritic conditions..." Yeda and Claiborne both teach that TNF is linked to arthritic conditions and thus there is clearly sufficient motivation to combine the cited prior art. One of ordinary skill in the art would have also have a reasonable expectation of success treating the instantly disclosed conditions with enoxaparin since Yeda teaches that LMWH's such as enoxaparin inhibit TNF secretion.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeda Research and Development WO 92/19249 (Yeda) and Claiborne et al. US 6,291,457 (Claiborne) in combination.

Claims 31-37 are drawn to a method of treating a disorder comprising administering to a subject a therapeutically effective amount of enoxaparin, wherein the disorder is one or more of a wound healing disturbance, a disorder of the locomotor system, osteoarthroses, spondyloses, chondrolysis, collagenoses, or arthropathies.

Yeda teaches the treatment of pathological processes involving the induction of TNF-α secretion using a pharmaceutically acceptable carrier and a low molecular weight heparin (LMWH) (Abstract). The LMWH is present in a low effective dose and is administered at intervals of about 5-8 days. The LMWH is capable of inhibiting *in vitro* TNF-α secretion by resting T cells and/or macrophages in response to T cell-specific antigens, mitogens, macrophages activators, disrupted extracellular matrix (dECM), laminin, fibronectin, and the like. TNF-α is involved in the pathogenesis of many undesirable inflammatory conditions in autoimmune diseases, graft rejection, vasculitis and atherosclerosis (page 3, lines 18-25). For these reasons, ways have been sought to regulate the secretion of TNF-α as a means to control a variety of diseases. The pharmaceutical composition may be administered in any manner as dictated by the particular application at hand including, but not limited to, enteral administration (including oral) or parenteral administration (including topical or inhalation with the aid of aerosols) (page 7, line 34 to page 8, line 24). The compositions typically contain a single low dose unit of less than 5 mg LMWH, preferably from about 0.3 to about 3 mg, and most preferably contain from 1 to 1.5 mg. LMWHs to be used in the method include enoxaparin which is commercially available (page 10, line 15 to page 11, line 34).

Yeda differs from the instantly claimed invention in that Yeda does not explicitly teach the treatment of osteoarthroses, spondyloses, chondrolysis, collagenoses, and arthropaties; however, these deficiencies would have been obvious to one of ordinary skill in the art at the time the invention was made.

Claiborne teaches that excessive or unregulated TNF production or activity has been implicated in mediating or exacerbating rheumatoid arthritis, rheumatoid sponylitis, osteoarthritis, gouty arthritis, and other arthritic conditions, sepsis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, adult respiratory distress syndrome, cerebral malaria, chronic pulmonary inflammation disease, silicosis, pulmonary sarcosis, bone resorption diseases, reperfusion injury, graft v. host rejection, allograft rejections, fever and myalgia due to infection, cachexia secondary to infection or malignancy, cachexia secondary to AIDS, AIDS related complex (ARC), keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis and pyresis (column 1, lines 40-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat one or more of osteoarthroses, spondyloses, chondrolysis, collagenoses, arthropaties, wound healing disturbances, and disorder of locomotor system by administering to a subject a therapeutically effective amount of enoxaparin. Yeda teaches the treatment of pathological processes involving the induction of TNF-α secretion using enoxaparin within the dosage range instantly claimed. Although Yeda does not explicitly teach the treatment of osteoarthroses, spondyloses, chondrolysis, collagenoses, or arthropaties, it would have been obvious to one of ordinary skill in the

art at the time of the invention to do so since Claiborne teaches that excessive or unregulated TNF production or activity has been implicated in mediating or exacerbating a variety of conditions including rheumatoid arthritis, rheumatoid sponylitis, osteoarthritis, gouty arthritis, and other arthritic conditions, reperfusion injury, graft v. host rejection, allograft rejections, fever and myalgia due to infection, keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis and pyresis. One of ordinary skill in the art would have been motivated to do so in view of the links between the induction of TNF-α secretion and the instantly claimed pathological processes.

Conclusion

12. Claims 1, 3-8, and 26-37 are pending. Claims 1, 3-8, and 26-37 are rejected. No claims are allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Oku et al. US 4,889,851; Oku et al. EP 0243173 A2; and Robins EP 0507831 B1 are cited to show that one of ordinary skill in the art at the time of the invention would be aware that rheumatoid arthritis was a condition characterized by a disturbance of bone metabolism.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

ptl